



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/621,428	07/16/2003	Dieter Heindl	022101-003900US	8931
41504	7590	08/21/2006	EXAMINER	
TOWNSEND AND TOWNSEND AND CREW, LLP 2 EMBARCADERO CENTER, 8TH FLOOR SAN FRANCISCO, CA 94111			LU, FRANK WEI MIN	
			ART UNIT	PAPER NUMBER
			1634	

DATE MAILED: 08/21/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/621,428

Applicant(s)

HEINDL ET AL.

Examiner

Frank W Lu

Art Unit

1634

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM
THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 12 June 2006.
2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☐ Claim(s) 18-23,32,34,35 and 37-49 is/are pending in the application.
4a) Of the above claim(s) _____ is/are withdrawn from consideration.
5) ☒ Claim(s) 44 is/are allowed.
6) ☒ Claim(s) 18-23,32,34,35,37-43 and 45-49 is/are rejected.
7) ☐ Claim(s) _____ is/are objected to.
8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
10) ☒ The drawing(s) filed on 16 July 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

1. Applicant's response to the office action filed on June 12, 2006 has been entered. The claims pending in this application are claims 18-23, 32, 34, 35, and 37-49. Rejection and/or objection not reiterated from the previous office action are hereby withdrawn in view of amendment filed on June 12, 2006.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. New Matter

Claims 20-23, 35, 37-39, 41, 43, and 45-49 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Although the specification describes that a pair of FRET hybridization probes hybridizing adjacently to each other on a target nucleic acid as pointed out by applicant (see page 3, lines 5-23 and page 8, lines 12-15), the specification does not describe a solution comprising 3 oligonucleotide as recited in claim 20-23, 35, 37-39, 41, 43, and 44. Although the specification describes to lyophilize PCR primers and probes as pointed out by applicant (see page 11, lines

Art Unit: 1634

19-20), the specification does not describe a lyophilized solution comprising a plurality of FRET hybridization probes as recited in claims 45, 47, and 49 and a lyophilized solution comprising 3 oligonucleotides recited in claims 46, 48, and 49.

MPEP 2163.06 notes "If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. *In re Rasmussen*, 650 F.2d 1212, 211 USPQ 323 (CCPA 1981)." MPEP 2163.02 teaches that "Whenever the issue arises, the fundamental factual inquiry is whether a claim defines an invention that is clearly conveyed to those skilled in the art at the time the application was filed...If a claim is amended to include subject matter, limitations, or terminology not present in the application as filed, involving a departure from, addition to, or deletion from the disclosure of the application as filed, the examiner should conclude that the claimed subject matter is not described in that application."

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

5. Claims 18 and 19 are rejected under 35 U.S.C. 102(e) as being anticipated by Bao *et al.*, (US Patent No. 5,866,336, published on February 2, 1999).

Regarding claim 18, since Bao *et al.*, teach a composition for detection of a subject nucleic acid comprising a first nucleic acid probe that hybridizes to a first nucleic acid target sequence on the subject nucleic acid, forms a stem-loop structure when not bound to the first nucleic acid target sequence, and incorporates a resonance energy transfer donor moiety; and a second nucleic acid probe that hybridizes to a second nucleic acid target sequence on the subject

Art Unit: 1634

nucleic acid, forms a stem-loop structure when not bound to the second nucleic acid target sequence, and incorporates a resonance energy transfer acceptor moiety, wherein the first nucleic acid target sequence and the second nucleic acid target sequence are separated by a number of nucleotides on the subject nucleic acid such that a resonance energy transfer signal from interaction between the donor moiety of the first nucleic acid probe and the acceptor moiety of the second nucleic acid probe can be detected to determine hybridization of both the first nucleic acid probe and the second nucleic acid probe to the subject nucleic acid, wherein the first nucleic acid probe further incorporates a quencher moiety, such that an interaction between the donor moiety of the first nucleic acid probe and the quencher moiety can be detected to differentiate between the first nucleic acid probe in the stem-loop structure and non-stem-loop structure, and wherein the second nucleic acid probe further incorporates a quencher moiety, such that an interaction between the acceptor moiety of the second nucleic acid probe and the quencher moiety can be detected to differentiate between the second nucleic acid probe in the stem-loop structure and non-stem-loop structure (claims 1-3 and 43 in columns 53 and 56 and Figures 1 and 2), and claims 18 and 22 do not require that a first single stranded oligonucleotide is a complete single stranded oligonucleotide, Bao *et al.*, disclose that a solution comprising a plurality of fluorescence resonance energy transfer (FRET) hybridization probes comprising first oligonucleotide (ie., the partial single stranded first nucleic acid probe) carrying a FRET donor entity (ie., FAM, see claim 7 in column 54) and at least one second entity (ie., the quencher), said second entity being a compound (ie., DABCYL in Figure 2) which is capable of quenching fluorescence emission of said donor fluorescent entity (ie., FAM) and a second oligonucleotide

Art Unit: 1634

(ie., the partial single stranded second nucleic acid probe) carrying a FRET acceptor entity (ie., Cy3 in Figure 2) but not carrying a FRET donor entity as recited in claim 18.

Regarding claim 19, since Bao *et al.*, teach that FAM connects DABCYL by G-hydrogen bond-C (see Figures 12A and 12B), Bao *et al.*, disclose that the FRET donor entity (ie., FAM) and the second entity (ie., DABCYL) are carried on adjacent nucleotides of the first oligonucleotide (ie., the partial single stranded first nucleic acid probe) as recited in claim 19.

Regarding claim 22, since Bao *et al.*, teach a complex formed by a subject nucleic acid, a first nucleic acid probe and a second nucleic acid probe (see claim 1 in column 53 and claim 43 in column 56), Bao *et al.*, disclose further comprising a nucleic acid sample (ie., the subject nucleic acid).

Regarding claim 43, Bao *et al.*, teach a kit comprising the solution of claim 18 (see column 8, second paragraph).

Therefore, Bao *et al.*, teach all limitations recited in claims 18, 19, 22, and 43.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any

Art Unit: 1634

evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claim 23 is rejected under 35 U.S.C. 103(a) as being unpatentable over Bao *et al.*, as applied to claims 19, 20, 22, and 43 above, and further in view of Nazarenko *et al.*, (US Patent No. 5,866,336, published on February 2, 1999).

The teachings of Bao *et al.*, have been summarized previously, *supra*.

Bao *et al.*, do not disclose further comprising at least one other component selected from a group consisting of a nucleic acid amplification primer, a template dependent nucleic acid polymerase, at least one deoxynucleoside triphosphate and a buffer for template dependent nucleic acid amplification reaction as recited in claim 23. However, Bao *et al.*, indicate that their nucleic acid probes are used in amplification reactions as primers (see column 15, first paragraph).

Nazarenko *et al.*, teach an upstream hairpin primer and a reverse primer (see Figure 2).

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have made a solution recited in claim 23 by adding a nucleic acid amplification primer so that the nucleic acid amplification primer and one of nucleic acid probes taught by Bao *et al.*, form a primer pair in view of patents of Bao *et al.*, and Nazarenko *et al.*. One having ordinary skill in the art has been motivated to do so because Bao *et al.*, indicate that their nucleic acid probes are used in amplification reactions as primers (see column 15, first paragraph). One having ordinary skill in the art at the time the invention was

Art Unit: 1634

made would have been a reasonable expectation of success to add a nucleic acid amplification primer so that the nucleic acid amplification primer and one of nucleic acid probes taught by Bao *et al.*, form a primer pair.

8. Claims 32 and 34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bao *et al.*, as applied to claims 19, 20, 22, and 43 above, and further in view of Wittwer *et al.*, (US Patent No. 6,635,427, priority date: August 11, 2000).

The teachings of Bao *et al.*, have been summarized previously, *supra*.

Regarding claim 33, in view of claims 18 and 32 and above rejection under 35 U.S.C 102, Bao *et al.*, teach all limitations of claim 32 except a nitroindole moiety.

Regarding claim 34, since claims 19 and 34 are identical, Bao *et al.*, teach claim 34.

Wittwer *et al.*, teach a single-stranded oligonucleotide carrying a FRET donor entity and a nitroindole moiety capable of quenching fluorescence of said FRET donor entity (see column 43, claims 1 and 2).

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have made a solution comprising a first single-stranded oligonucleotide carrying a FRET donor entity and a nitroindole moiety capable of quenching fluorescence of said FRET donor entity in view of the patents of Bao *et al.*, and Wittwer *et al.*. One having ordinary skill in the art would have been motivated to do so because Wittwer *et al.*, have taught a first single-stranded oligonucleotide carrying a FRET donor entity and a nitroindole moiety capable of quenching fluorescence of said FRET donor entity and the simple substitution of one kind of fluorescent quencher (ie., Dabayl taught by Bao *et al.*,) from another

Art Unit: 1634

kind of fluorescent quencher (ie., a nitroindole moiety) during the process of making a solution recited in claim 32, in the absence of convincing evidence to the contrary, would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made.

Furthermore, the motivation to make the substitution cited above arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making the obviousness rejection comes from the M.P.E.P. at 2144.07 and 2144.09.

Also note that there is no invention involved in combining old elements in such a manner that these elements perform in combination the same function as set forth in the prior art without giving unobvious or unexpected results. *In re Rose* 220 F.2d. 459, 105 USPQ 237 (CCPA 1955).

9. Claim 42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bao *et al.*, in view of Wittwer *et al.*, as applied to claims 19, 20, 22, 32, 34, and 43 above, and further in view of Segev (US Patent No. 5,437,977, published on August 1, 1995).

The teachings of Bao *et al.*, and Wittwer *et al.*, have been summarized previously, *supra*. In view of claims 32 and 42, since a plurality of FRET hybridization probes recited in claims 32 and 42 are identical, Bao *et al.*, in view of Wittwer *et al.*, teach a plurality of FRET hybridization probes recited in claim 42.

Bao *et al.*, and Wittwer *et al.*, do not disclose a solid support comprising a plurality of FRET hybridization probes as recited in claim 40.

Segev teaches that immobilizing the target nucleic acid molecule occurs before hybridizing the primary probe to the target nucleic acid molecule. The advantage of

Art Unit: 1634

immobilizing the target nucleic acid molecule is that the unhybridized labeled molecules is separated from the immobilized complex prior to detection, thereby reducing the background and increasing the signal-noise ratio (see column 17, lines 3-14).

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have made a support comprising a plurality of FRET hybridization probes recited in claim 42 by immobilizing the subject nucleic acid taught by Bao *et al.*, to a support before hybridization in order to form a support comprising the plurality of FRET hybridization probes and the subject nucleic acid in view of patents of Bao *et al.*, and Wittwer *et al.*, and Segev. One having ordinary skill in the art has been motivated to do so because Segev suggests that immobilizing the target nucleic acid molecule before hybridization assay would enhance separation of unhybridized molecules from the immobilized complex prior to detection and thereby reducing the background and increasing the signal-noise ratio (see column 17, lines 3-14). One having ordinary skill in the art at the time the invention was made would have been a reasonable expectation of success to make a support comprising a plurality of FRET hybridization probes as recited in claim 42.

10. Claim 40 is rejected under 35 U.S.C. 103(a) as being unpatentable over Bao *et al.*, as applied to claims 19, 20, 22, and 43 above, and further in view of Segev.

The teachings of Bao *et al.*, have been summarized previously, *supra*. In view of claims 18 and 40, since a plurality of FRET hybridization probes recited in claims 18 and 40 are identical, Bao *et al.*, teach a plurality of FRET hybridization probes recited in claim 40.

Bao *et al.*, do not disclose a solid support comprising a plurality of FRET hybridization

Art Unit: 1634

probes as recited in claim 40.

Segev teaches that immobilizing the target nucleic acid molecule occurs before hybridizing the primary probe to the target nucleic acid molecule. The advantage of immobilizing the target nucleic acid molecule is that the unhybridized labeled molecules is separated from the immobilized complex prior to detection, thereby reducing the background and increasing the signal-noise ratio (see column 17, lines 3-14).

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have made a support comprising a plurality of FRET hybridization probes recited in claim 40 by immobilizing the subject nucleic acid taught by Bao *et al.*, to a support before hybridization in order to form a support comprising the plurality of FRET hybridization probes and the subject nucleic acid in view of patents of Bao *et al.*, and Segev. One having ordinary skill in the art has been motivated to do so because Segev suggests that immobilizing the target nucleic acid molecule before hybridization assay would enhance separation of unhybridized molecules from the immobilized complex prior to detection and thereby reducing the background and increasing the signal-noise ratio (see column 17, lines 3-14). One having ordinary skill in the art at the time the invention was made would have been a reasonable expectation of success to make a support comprising a plurality of FRET hybridization probes as recited in claim 40.

Conclusion

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

12. Claim 44 is allowed over prior art.

13. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CAR § 1.6(d)). The CM Fax Center number is (571)273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Lu, Ph.D., whose telephone number is (571)272-0746. The examiner can normally be reached on Monday-Friday from 9 A.M. to 5 P.M.

Art Unit: 1634

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached on (571)272-0735.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

August 15, 2006

A handwritten signature in black ink, appearing to read 'Frank Lu', is written above the printed name.

FRANK LU
PRIMARY EXAMINER